

cl 2(6)

(FILE 'HOME' ENTERED AT 13:16:28 ON 02 DEC 2004)

FILE 'CAPLUS, MEDLINE' ENTERED AT 13:18:11 ON 02 DEC 2004
L1 81 FILE CAPLUS
L2 140 FILE MEDLINE
TOTAL FOR ALL FILES
L3 221 S ((HIV (3W) (REVERSE TRANSCRIPTASE)) OR NTRI) AND RESISTANCE A
L4 1 FILE CAPLUS
L5 1 FILE MEDLINE
TOTAL FOR ALL FILES
L6 2 S L3 AND (184 (3A) ((G OR GLY) OR (L OR LEU)))

FILE 'CAPLUS' ENTERED AT 13:56:29 ON 02 DEC 2004
L7 4 S (129:15939 OR 124:219374 OR 123:74260 OR 122:230221)/DN

FILE 'CAPLUS, MEDLINE' ENTERED AT 14:09:40 ON 02 DEC 2004
L8 1 FILE CAPLUS
L9 0 FILE MEDLINE
TOTAL FOR ALL FILES
L10 1 S L3 AND (215 (3A) ((V OR VAL)))
L11 0 FILE CAPLUS
L12 0 FILE MEDLINE
TOTAL FOR ALL FILES
L13 0 S L3 AND (118 (3A) ((I OR ILE)))
L14 3 FILE CAPLUS
L15 2 FILE MEDLINE
TOTAL FOR ALL FILES
L16 5 S L3 AND (44 (3A) ((A OR ALA) OR (D OR GLU)))
L17 1 DUPLICATE REMOVE L6 (1 DUPLICATE REMOVED)

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* * * * * * * * * * * * * Welcome to STN International * * * * * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 SEP 01 INPADOC: New family current-awareness alert (SDI) available
NEWS 4 SEP 01 New pricing for the Save Answers for SciFinder Wizard within
STN Express with Discover!
NEWS 5 SEP 01 New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
NEWS 6 SEP 27 STANDARDS will no longer be available on STN
NEWS 7 SEP 27 SWETSCAN will no longer be available on STN
NEWS 8 OCT 28 KOREAPAT now available on STN
NEWS 9 NOV 18 Current-awareness alerts, saved answer sets, and current
search transcripts to be affected by CERAB, COMPUAB, ELCOM,
and SOLIDSTATE reloads
NEWS 10 NOV 30 PHAR reloaded with additional data
NEWS 11 DEC 01 LISA now available on STN

NEWS EXPRESS OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:16:28 ON 02 DEC 2004

=> file caplus,medline
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 0.63 0.63

FILE 'CAPLUS' ENTERED AT 13:18:11 ON 02 DEC 2004
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FILE 'MEDLINE' ENTERED AT 13:18:11 ON 02 DEC 2004

=> s ((HIV (3w) (reverse transcriptase)) or NTRI) and resistance and (44 or 69 or 118 or 184)
L1 81 FILE CAPLUS
L2 140 FILE MEDLINE

TOTAL FOR ALL FILES
L3 221 ((HIV (3W) (REVERSE TRANSCRIPTASE)) OR NTRI) AND RESISTANCE AND
(44 OR 69 OR 118 OR 184)

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```
=> duplicate remove
ENTER L# LIST OR (END):13
DUPLICATE PREFERENCE IS 'CAPLUS, MEDLINE'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L3
L4      152 DUPLICATE REMOVE L3 (69 DUPLICATES REMOVED)
```

```
=> del 14
DELETE L4? (Y)/N:y
```

```
=> s l3 and (184 (3a) ((G or Gly) or (L or Leu))
UNMATCHED LEFT PARENTHESIS 'AND (184'
The number of right parentheses in a query must be equal to the
number of left parentheses.
```

```
=> s l3 and (184 (3a) ((G or Gly) or (L or Leu)))
L4      1 FILE CAPLUS
L5      1 FILE MEDLINE
```

```
TOTAL FOR ALL FILES
L6      2 L3 AND (184 (3A) ((G OR GLY) OR (L OR LEU)))
```

```
=> d
```

```
L6      ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
Full Text
AN 1996:491295 CAPLUS
DN 125:189243
TI Mutational studies of human immunodeficiency virus type 1 reverse
transcriptase: the involvement of residues 183 and 184 in the fidelity
of DNA synthesis
AU Bakhashvili, Mary; Avidan, Orna; Hizi, Amnon
CS Department of Cell Biology and Histology, Sackler School of Medicine, Tel
Aviv University, Tel Aviv-Jaffa, 69978, Israel
SO FEBS Letters (1996), 391(3), 257-262
CODEN: FEBBLA; ISSN: 0014-5793
PB Elsevier
DT Journal
LA English
```

```
=> d bib,abs
```

```
L6      ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
Full Text
AN 1996:491295 CAPLUS
DN 125:189243
TI Mutational studies of human immunodeficiency virus type 1 reverse
transcriptase: the involvement of residues 183 and 184 in the fidelity
of DNA synthesis
AU Bakhashvili, Mary; Avidan, Orna; Hizi, Amnon
CS Department of Cell Biology and Histology, Sackler School of Medicine, Tel
Aviv University, Tel Aviv-Jaffa, 69978, Israel
SO FEBS Letters (1996), 391(3), 257-262
CODEN: FEBBLA; ISSN: 0014-5793
PB Elsevier
DT Journal
LA English
AB The high error rates characteristic of human immunodeficiency virus type-1
reverse transcriptase (HIV-1 RT) are a presumptive source of the viral
hypermutability that impedes prevention and therapy of acquired
immunodeficiency syndrome (AIDS). We have analyzed two mutants of HIV-1
```

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RT by conducting a comparative study of the accuracy of DNA synthesis. Each mutant bears a single amino acid substitution adjacent to the two aspartic acid residues at positions 185 and 186 in the highly conserved DNA polymerase active site. The first mutant, Met 184→Leu (M184L), displays a marked redn. in both misinsertion and mispair extension, suggesting a fidelity of DNA synthesis significantly higher than that of the wild-type HIV-1 RT. The second mutant, Tyr 183→Phe (Y183F), shows a decrease in mispair extension with no significant change in misincorporation. Thus, the overall pattern of error-proneness of DNA synthesis is: wild-type HIV-1 RT > Y183F > M184L. Taken together, it is possible that residues 183 and 184 contribute to the low fidelity of DNA synthesis characteristic of the reverse transcriptases of HIV-1, HIV-2 and possibly, of other lentiviruses. Our observations may bear on the nature of potential mutations responsible for resistance to the nucleoside analogs used in chemotherapy of AIDS.

=> d au,so

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
AU Bakhanashvili, Mary; Avidan, Orna; Hizi, Amnon
SO FEBS Letters (1996), 391(3), 257-262
CODEN: FEBLAL; ISSN: 0014-5793

=> d au,so

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
AU Bakhanashvili, Mary; Avidan, Orna; Hizi, Amnon
SO FEBS Letters (1996), 391(3), 257-262
CODEN: FEBLAL; ISSN: 0014-5793

=> file caplus

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|--|------------------|---------------|
| FULL ESTIMATED COST | 57.75 | 58.38 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | -0.70 | -0.70 |

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FILE LAST UPDATED: 1 Dec 2004 (20041201/ED)

This file contains CAS Registry Numbers for easy and accurate

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substance identification.

=> s (129:15939 or 124:219374 or 123:74260 or 122:230221)/dn
1 129:15939/DN
1 124:219374/DN
1 123:74260/DN
1 122:230221/DN
L7 4 (129:15939 OR 124:219374 OR 123:74260 OR 122:230221)/DN

=> d au,so 1-4

L7 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AU Cushman, Mark; Casimiro-Garcia, Agustin; Hejchman, Elzbieta; Ruell,
Jeffrey A.; Huang, Mingjun; Schaeffer, Catherine A.; Williamson, Karen;
Rice, William G.; Buckheit, Robert W., Jr.
SO Journal of Medicinal Chemistry (1998), 41(12), 2076-2089
CODEN: JMCMAR; ISSN: 0022-2623

L7 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AU Buckheit, Robert W., Jr.; Kinjerski, Tracy L.; Fliakas-Boltz, Valerie;
Russell, Julie D.; Stup, Tracy L.; Pallansch, Luke A.; Brouwer, Walter G.;
Dao, Dong C.; Harrison, W. Ashley; et al.
SO Antimicrobial Agents and Chemotherapy (1995), 39(12), 2718-27
CODEN: AMACQ; ISSN: 0066-4804

L7 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AU Buckheit, Robert W., Jr.; Fliakas-Boltz, VAlerie; Yeagy-Bargo, Sharon;
Weislow, Owen; Mayers, Douglas L.; Boyer, Paul L.; Hughes, Stephen H.;
Pan, Bai-Chuan; Chu, Shih-Hsi; et al.
SO Virology (1995), 210(1), 186-93
CODEN: VIRLAX; ISSN: 0042-6822

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AU Seki, M.; Sadakata, Y.; Yuasa, S.; Baba, M.
SO Antiviral Chemistry Chemotherapy (1995), 6(2), 73-9
CODEN: ACCHEH; ISSN: 0956-3202

=> d dn,au,so 1-4

L7 ANSWER 1 OF 4 CAPIUS COPYRIGHT 2004 ACS on STN
DN 129:15939
AU Cushman, Mark; Casimiro-Garcia, Agustin; Hejchman, Elzbieta; Ruell,
Jeffrey A.; Huang, Mingjun; Schaeffer, Catherine A.; Williamson, Karen;
Rice, William G.; Buckheit, Robert W., Jr.
SO Journal of Medicinal Chemistry (1998), 41(12), 2076-2089
CODEN: JMCMAR; ISSN: 0022-2623

L7 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
DN 124:219374
AU Buckheit, Robert W., Jr.; Kinjerski, Tracy L.; Fliakas-Boltz, Valerie;
Russell, Julie D.; Stup, Tracy L.; Pallansch, Luke A.; Brouwer, Walter G.;
Dao, Dong C.; Harrison, W. Ashley; et al.
SO Antimicrobial Agents and Chemotherapy (1995), 39(12), 2718-27
CODEN: AMACQ; ISSN: 0066-4804

L7 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
DN 123:74260
AU Buckheit, Robert W., Jr.; Fliakas-Boltz, VAlerie; Yeagy-Bargo, Sharon;
Weislow, Owen; Mayers, Douglas L.; Boyer, Paul L.; Hughes, Stephen H.;
Pan, Bai-Chuan; Chu, Shih-Hsi; et al.

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SO Virology (1995), 210(1), 186-93
CODEN: VIRLAX; ISSN: 0042-6822

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
DN 122:230221
AU Seki, M.; Sadakata, Y.; Yuasa, S.; Baba, M.
SO Antiviral Chemistry Chemotherapy (1995), 6(2), 73-9
CODEN: ACCHEH; ISSN: 0956-3202

=> d4 bib,abs

D4 IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (>).

=> d 4 bib,abs

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

Full Text

AN 1995:445027 CAPLUS

DN 122:230221

TI Isolation and characterization of human immunodeficiency virus type-1 mutants resistant to the non-nucleotide reverse transcriptase inhibitor MKC-442

AU Seki, M.; Sadakata, Y.; Yuasa, S.; Baba, M.

CS Laboratory of Bioscience, Mitsubishi Kasei Corp., Yokohama, 227, Japan

SO Antiviral Chemistry Chemotherapy (1995), 6(2), 73-9

CODEN: ACCHEH; ISSN: 0956-3202

PB Blackwell

DT Journal

LA English

AB MKC-442, 6-benzyl-1-ethoxymethyl-5-isopropyluracil (I-EBU), is a potent and selective non-nucleoside inhibitor of human immunodeficiency virus type-1 (HIV-1) reverse transcriptase (RT). Nevirapine, another non-nucleoside RT inhibitor (NNRTI), is assocd. with rapid emergence of drug-resistant variants during in vitro passages of HIV-1. The emergence of resistant viruses to MKC-442 or nevirapine was examd. in vitro. MT-4 cells infected with a clin. isolate (HE) of HIV-1 were cultivated in medium contg. excess concns. of these drugs, and the drug susceptibilities of the breakthrough viruses recovered from the medium were measured. Although nevirapine lost its antiviral activity after six passages, a delay in the emergence of fully resistant viruses was obsd. for MKC-442. Two resistant clones for each drug were isolated and nucleotide sequences within the RT region were analyzed. An amino acid substitution at position 181 (Tyr to Cys) was found, with addnl. substitutions at positions 103 (Lys to Arg) and 108 (Val to Ile) in the MKC-442-resistant viruses. These clones showed various susceptibilities to MKC-442, and cross-resistance to other NNRTIs but not to AZT. These results suggest that the major binding site of MKC-442 on the HIV-1 RT is the tyrosine residue common to these NNRTIs, and that drug resistance to NNRTIs is dependent on both the quality and the quantity of mutations within the HIV-1 RT gene.

=> d his

(FILE 'HOME' ENTERED AT 13:16:28 ON 02 DEC 2004)

FILE 'CAPLUS, MEDLINE' ENTERED AT 13:18:11 ON 02 DEC 2004

L1 81 FILE CAPLUS
L2 140 FILE MEDLINE

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TOTAL FOR ALL FILES
L3 221 S ((HIV (3W) (REVERSE TRANSCRIPTASE)) OR NTRI) AND RESISTANCE A
L4 1 FILE CAPLUS
L5 1 FILE MEDLINE
TOTAL FOR ALL FILES
L6 2 S L3 AND (184 (3A) ((G OR GLY) OR (L OR LEU)))

L7 FILE 'CAPLUS' ENTERED AT 13:56:29 ON 02 DEC 2004
4 S (129:15939 OR 124:219374 OR 123:74260 OR 122:230221) /DN

| | | |
|--|------------|---------|
| => file caplus,medline | | |
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| FULL ESTIMATED COST | ENTRY | SESSION |
| | 27.99 | 86.37 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| CA SUBSCRIBER PRICE | ENTRY | SESSION |
| | -0.70 | -1.40 |

FILE 'CAPLUS' ENTERED AT 14:09:40 ON 02 DEC 2004
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FILE 'MEDLINE' ENTERED AT 14:09:40 ON 02 DEC 2004

```
=> s 13 and (215 (3a) ((V or Val) ))  
L8           1 FILE CAPLUS  
L9           0 FILE MEDLINE
```

TOTAL FOR ALL FILES
L10 1 L3 AND (215 (3A) ((V OR VAL)))

三> d

L10 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
Full Text
AN 2000:712654 CAPLUS
DN 133:262274
TI HIV protease and reverse transcriptase gene mutation detection
method via PCR and hybridization
IN Shimada, Kazunori
PA Genome Science Kenkyusho K. K., Japan
SO Jpn. Kokai Tokkyo Koho, 19 pp.
COPR 2004 STN International

CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--------------------|------|----------|-----------------|----------|
| JP 2000279197 | A2 | 20001010 | JP 1999-92269 | 19990331 |
| PRAT JP 1999-92269 | | 19990331 | | |

```
=> s l3 and (118 (3a) ((I or Ille) ))  
L11          0 FILE CAPPLUS  
L12          0 FILE MEDLINE
```

TOTAL FOR ALL FILES
L13 0 L3 AND (118 (3A) ((I OR II-E)))

=> s 13 and (44 (3a) ((A or Ala) or (D or Glu))

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UNMATCHED LEFT PARENTHESIS 'AND (44'

The number of right parentheses in a query must be equal to the number of left parentheses.

```
=> s l3 and (44 (3a) ((A or Ala) or (D or Glu)))
L14      3 FILE CAPLUS
L15      2 FILE MEDLINE
```

TOTAL FOR ALL FILES

```
L16      5 L3 AND (44 (3A) ((A OR ALA) OR (D OR GLU)))
```

=> duplicate remove n

ENTER L# LIST OR (END):l16

'N' IS NOT VALID. VALID FILE NAMES ARE 'CAPLUS, MEDLINE'

You have entered a file name of duplicates to keep that is not referenced by any of the L#s specified for this DUPLICATE command.

The file names of duplicates that can be kept are listed above.

Please enter one of these file names.

ENTER FILE NAMES OF DUPLICATES TO KEEP:end

=> duplicate remove 16

DUPLICATE PREFERENCE IS 'CAPLUS, MEDLINE'

KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L6

```
L17      1 DUPLICATE REMOVE L6 (1 DUPLICATE REMOVED)
```

=> d l16 bib,kwic 1-5

L16 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
Full Text

AN 2003:986848 CAPLUS

DN 141:116470

TI An open-label assessment of TMC 125-a new, next-generation NNRTI, for 7 days in HIV-1 infected individuals with NNRTI **resistance**

AU Gazzard, Brian G.; Pozniak, Anton L.; Rosenbaum, Willy; Yeni, G. Patrick; Staszewski, Schlomo; Arasteh, Keikawus; De Dier, Karin; Peeters, Monika; Woodfall, Brian; Stebbing, Justin; van't Klooster, Gerben A.

CS Chelsea and Westminster Hospital, London, UK

SO AIDS (London, United Kingdom) (2003), 17(18), F49-F54
CODEN: AIDSET; ISSN: 0269-9370

PB Lippincott Williams Wilkins

DT Journal

LA English

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI An open-label assessment of TMC 125-a new, next-generation NNRTI, for 7 days in HIV-1 infected individuals with NNRTI **resistance**

AB Summary: The development of **resistance** to any of the currently licensed non-nucleoside reverse transcriptase inhibitors (NNRTI) invariably leads to cross-**resistance** to the drugs in that class. New NNRTI, that have the promise of being active even when such 'signature' mutations are present, are in development. Such novel therapies could be effective after current NNRTI failure as there would probably be no cross-**resistance**. We assessed the short-term efficacy and safety of a next generation NNRTI, TMC 125, a diarylpyrimidine deriv. that has in vitro activity against NNRTI resistant HIV-1. TMC 125 was studied in HIV-1 infected patients with high-level phenotypic NNRTI **resistance** in an open-label phase IIa trial. Methods: Sixteen individuals receiving an NNRTI-contg. antiretroviral regimen (efavirenz or nevirapine) with an HIV-1 RNA viral load of > 2000 copies/mL and phenotypic **resistance** to NNRTI, received TMC 125 for 7 days, as a substitute for their current NNRTI in their failing therapy. Full pharmacokinetic profiles were

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investigated. Findings: The primary end point-viral load decay rate per day - was 0.13 log₁₀ RNA copies/mL per day. Over 7 days, we obsd. a median 0.89 log₁₀ decrease in HIV-1 viral load; seven individuals (44%) had a decrease of > 1 log₁₀. The most significant adverse effects were grade I diarrhea (31%) and a mild headache (25%). Steady-state drug levels were achieved by day 6. Interpretation: TMC 125, a next generation NNRTI, is well tolerated and demonstrates significant and rapid antiviral activity in patients with high levels of phenotypic NNRTI **resistance** to current NNRTI.

ST non nucleoside reverse transcriptase inhibitor TMC125 pharmacokinetics HIV antiAIDS; antiviral **resistance** HIV antiAIDS non nucleoside reverse transcriptase inhibitor

IT Drug **resistance**
(antiviral; new generation NNRTI TMC-125 is well tolerated with significant antiviral activity in HIV-1 patient even in presence of mutations conferring high level of phenotypic **resistance** to efavirenz and nevirapine)

IT Anti-AIDS agents
Human
Human immunodeficiency virus 1
Phenotypes
(new generation NNRTI TMC-125 is well tolerated with significant antiviral activity in HIV-1 patient even in presence of mutations conferring high level of phenotypic **resistance** to efavirenz and nevirapine)

IT Viral RNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(new generation NNRTI TMC-125 is well tolerated with significant antiviral activity in HIV-1 patient even in presence of mutations conferring high level of phenotypic **resistance** to efavirenz and nevirapine)

IT Antiviral agents
(**resistance** to; new generation NNRTI TMC-125 is well tolerated with significant antiviral activity in HIV-1 patient even in presence of mutations conferring high level of phenotypic **resistance** to efavirenz and nevirapine)

IT 269055-15-4, TMC 125
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new generation NNRTI TMC-125 is well tolerated with significant antiviral activity in HIV-1 patient even in presence of mutations conferring high level of phenotypic **resistance** to efavirenz and nevirapine)

IT 129618-40-2, Nevirapine 136817-59-9, Delavirdine 154598-52-4, Efavirenz
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new generation NNRTI TMC-125 is well tolerated with significant antiviral activity in HIV-1 patient even in presence of mutations conferring high level of phenotypic **resistance** to efavirenz and nevirapine)

L16 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

Full Text

AN 2000:511498 CAPLUS

DN 134:80517

TI Evolution of lamivudine-resistant hepatitis B virus and HIV-1 in co-infected individuals. An analysis of the CAESAR study

AU Pillay, Deenan; Cane, Patricia A.; Ratcliffe, Daina; Atkins, Mark; Cooper, David

CS CAESAR Co-ordinating Committee, Public Health Laboratory Service Antiviral Susceptibility Reference Unit, Division of Immunity and Infection,

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University of Birmingham Medical School, Edgbaston, B15 2TT, UK
SO AIDS (London) (2000), 14(9), 1111-1116
CODEN: AIDSET; ISSN: 0269-9370
PB Lippincott Williams Wilkins
DT Journal
LA English
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB Lamivudine has potent activity against HIV-1 and hepatitis B virus (HBV). Co-infection with these 2 viruses is common, and this may therefore influence the choice of antiretroviral therapies. A cohort of co-infected patients treated with lamivudine were studied to evaluate the differential effects of lamivudine on the 2 viral populations within the same individual after 44-52 wk of therapy. Retrospective virol. anal. of an HIV-1/HBV co-infected lamivudine cohort derived from a randomized, placebo-controlled study of lamivudine in HIV infection, the CAESAR study. 5 Of 13 patients with HBV viral load >10,000 copies/mL after 44-52 wk of lamivudine therapy had genotypic drug **resistance**. 4 Of these 5 had a rebound of viral replication over the period of study and in 1 case this was assocd. with an alanine transaminase serum elevation. 10 Of the 13 patients had a 44-52 wk HIV viral load >1000 copies/mL, all of whom also had HIV **reverse transcriptase** M184V or M184I mutations. Extrapolating these results to the population yields an estd. 1-yr incidence of drug-resistant HBV of at least 14% in lamivudine-treated HIV-1/HBV co-infected patients. The clin. and virol. benefit of HBV lamivudine monotherapy in co-infected patients should be balanced against the potential for emergence of drug **resistance**. Further, these data suggest that the determinants of HIV and HBV drug **resistance** are different and that parallel evolution, rather than co-evolution of HBV and HIV-1 in co-infected individuals occurs.
ST lamivudine drug **resistance** hepatitis B virus HIV
IT Antiviral agents
 (**resistance** to; lamivudine-resistant hepatitis B virus and HIV-1 in co-infected individuals)

L16 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
Full Text
AN 1996:568526 CAPLUS
DN 125:264641
TI Nevirapine: a review of its development, pharmacological profile and potential for clinical use
AU Murphy, Robert L.; Montaner, Julio
CS Northwestern University, Chicago, IL, USA
SO Expert Opinion on Investigational Drugs (1996), 5(9), 1183-1199
CODEN: EOIDER; ISSN: 0967-8298
PB Ashley Publications
DT Journal; General Review
LA English
AB A review with 44 refs. Nevirapine, a dipyridodiazepinone, is the prototypic member of a class of antiretroviral compds. referred to as nonnucleoside reverse transcriptase inhibitors. Nevirapine is a potent and selective noncompetitive inhibitor of the reverse transcriptase enzyme, an important therapeutic target for the treatment of HIV-1 infection. The activity of nevirapine does not compete with template or nucleoside triphosphates, nor does it inhibit HIV-2 **reverse transcriptase** or any of the human DNA polymerases. In completed clin. studies, nevirapine has demonstrated antiretroviral activity both as monotherapy and in combination with nucleoside analogs. When administered with zidovudine or the combination zidovudine/didanosine, the antiviral effect has been profound and sustained. A favorable antiviral effect and CD4⁺ lymphocyte response has been demonstrated in both adults and children, in patients experienced and naive to antiretroviral therapy as

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well as in those with baseline **resistance** to zidovudine. Nevirapine has a favorable pharmacokinetic profile, becomes widely distributed throughout body tissues including the central nervous system, and is active in the adult at an oral dose of 200 mg administered twice daily after a two week leak-in dose of 200 mg per day. There are no significant drug-drug interactions noted with the nucleoside reverse transcriptase inhibitors; however, because nevirapine induces cytochrome P 450 isoenzymes, the currently used protease inhibitors may undergo more rapid rates of metab. Other commonly used drugs, such as ketoconazole, dapsone, rifampin, rifabutin and trimethoprim-sulfamethoxazole, appear not to be significantly affected. **Resistance** to nevirapine is rapid when administered as a monotherapy but this is altered and made less clin. relevant when nevirapine is given in combination with one or more of the nucleosides. Nevirapine has a safety profile that does not overlap with overlap with other antiretroviral therapies, the most common treatment-limiting reaction being rash. Nevirapine is an active antiretroviral agent with excellent biodistribution and good potential for use in combination with other antiretrovirals across the spectrum of HIV disease as well as in selected populations.

L16 ANSWER 4 OF 5 MEDLINE on STN

Full Text

AN 2001571617 MEDLINE

DN PubMed ID: 11679154

TI HIV type 1 genetic diversity is a major obstacle for antiretroviral drug **resistance** hybridization-based assays.

AU Kijak G H; Rubio A E; Quarleri J F; Salomon H

CS National Reference Center for AIDS, Department of Microbiology, School of Medicine, University of Buenos Aires, 1121 Buenos Aires, Argentina.

SO AIDS research and human retroviruses, (2001 Oct 10) 17 (15) 1415-21.
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CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals; AIDS

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EM 200112

ED Entered STN: 20011029

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STN Columbus

Entered Medline: 20011221
TI HIV type 1 genetic diversity is a major obstacle for antiretroviral drug **resistance** hybridization-based assays.
AB Human immunodeficiency virus type 1 (HIV-1) is characterized by high genetic diversity. Current antiretroviral (ARV) drug **resistance** genotyping assays have been designed on the basis of the most prevalent sequence patterns circulating in the United States and . . . genetic diversity of HIV-1 forms circulating in Argentina and the lack of reactivity at codon 74 in an ARV drug **resistance** hybridization-based assay. Samples taken from 93 HIV-1-infected individuals of Buenos Aires, Argentina were studied. The reverse transcriptase (RT) region of . . . recombination analyses were carried out, showing that 52 of 93 (55.9%) samples belonged to subtype B, whereas 41 of 93 (44.1%) showed a (5') F1/B (3') subtype recombinant genomic structure. For codon 74 in the LiPA test, 4 of 52 (7.7%) B-subtype samples . . . recombinant samples ($p < 0.001$). The present data indicate that HIV-1 genetic diversity is a major obstacle for ARV drug **resistance** hybridization-based assays.
CT Check Tags: Human; Support, Non-U.S. Gov't
Base Sequence
DNA, Viral
***Drug Resistance, Viral: GE, genetics**
HIV-1: CL, classification
***HIV-1: GE, genetics**
***HIV-1 Reverse Transcriptase: GE, genetics**
Molecular Sequence Data
Nucleic Acid Hybridization: MT, methods
Phylogeny
Recombination, Genetic
***Variation (Genetics)**
CN 0 (DNA, Viral); EC 2.7.7.- (**HIV-1 Reverse Transcriptase**)

L16 ANSWER 5 OF 5 MEDLINE on STN

Full Text

AN 200109355 MEDLINE
DN PubMed ID: 10894274
TI Evolution of lamivudine-resistant hepatitis B virus and HIV-1 in co-infected individuals: an analysis of the CAESAR study. CAESAR co-ordinating committee.
AU Pillay D; Cane P A; Ratcliffe D; Atkins M; Cooper D
CS Division of Immunity and Infection, University of Birmingham Medical School, Edgbaston, UK.. D.Pillay@bham.ac.uk
SO AIDS (London, England), (2000 Jun 16) 14 (9) 1111-6.
Journal code: 8710219. ISSN: 0269-9370.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
LA English
FS Priority Journals; AIDS
EM 200010
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001025
AB . . . studied in order to evaluate the differential effects of lamivudine on the two viral populations within the same individual after 44-52 weeks of therapy. DESIGN AND METHODS: Retrospective virological analysis of an HIV-1/HBV co-infected lamivudine cohort derived from a randomized, placebo-controlled. . . lamivudine in HIV infection, the CAESAR study. RESULTS: Five of thirteen patients with HBV viral load > 10,000 copies/ml after 44-52 weeks of lamivudine therapy had genotypic drug **resistance**. Four of these five had a rebound of viral replication over the period of study and in one case this was associated with an alanine transaminase serum elevation. Ten of the thirteen patients had

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a 44-52 week HIV viral load > 1000 copies/ml, all of whom also had HIV reverse transcriptase M184V or M184I mutations. CONCLUSIONS: Extrapolating these results to the population yields an estimated 1-year incidence of drug-resistant HBV of . . . and virological benefit of HBV lamivudine monotherapy in co-infected patients should be balanced against the potential for emergence of drug resistance. Further, these data suggest that the determinants of HIV and HBV drug resistance are different and that parallel evolution, rather than co-evolution of HBV and HIV-1 in co-infected individuals occurs.

CT Check Tags: Human; Support, Non-U.S. Gov't
CD4 Lymphocyte Count
***Drug Resistance, Microbial**
HIV Infections: BL, blood
***HIV Infections: CO, complications**
HIV Infections: IM, immunology
HIV-1: GE, genetics
HIV-1: IP, isolation

=> d his

(FILE 'HOME' ENTERED AT 13:16:28 ON 02 DEC 2004)

FILE 'CAPLUS, MEDLINE' ENTERED AT 13:18:11 ON 02 DEC 2004

L1 81 FILE CAPLUS
L2 140 FILE MEDLINE
TOTAL FOR ALL FILES
L3 221 S ((HIV (3W) (REVERSE TRANSCRIPTASE)) OR NTRI) AND RESISTANCE A
L4 1 FILE CAPLUS
L5 1 FILE MEDLINE
TOTAL FOR ALL FILES
L6 2 S L3 AND (184 (3A) ((G OR GLY) OR (L OR LEU)))

FILE 'CAPLUS' ENTERED AT 13:56:29 ON 02 DEC 2004

L7 4 S (129:15939 OR 124:219374 OR 123:74260 OR 122:230221)/DN

FILE 'CAPLUS, MEDLINE' ENTERED AT 14:09:40 ON 02 DEC 2004

L8 1 FILE CAPLUS
L9 0 FILE MEDLINE
TOTAL FOR ALL FILES
L10 1 S L3 AND (215 (3A) ((V OR VAL)))
L11 0 FILE CAPLUS
L12 0 FILE MEDLINE
TOTAL FOR ALL FILES
L13 0 S L3 AND (118 (3A) ((I OR ILE)))
L14 3 FILE CAPLUS
L15 2 FILE MEDLINE
TOTAL FOR ALL FILES
L16 5 S L3 AND (44 (3A) ((A OR ALA) OR (D OR GLU)))
L17 1 DUPLICATE REMOVE L6 (1 DUPLICATE REMOVED)

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